18. (New) The composition according to claim 17, wherein the nontoxic synthetic substance that blocks the N-methyl-D-Aspartate receptor is selected from pyrroloquinoline quinone and cis-4-(phosphonomethyl)-2-piperidinecarboxylic acid.

19 (New) The composition according to claim 17, wherein there is present a substance that blocks a major intracellular consequence of N-methyl-D-aspartate receptor activation.

REMARKS

This Amendment responds to the Office Action dated February 5, 2003, which rejected claims 1-16 under 35 U.S.C. § 103 (a) as being unpatentable over applicants' disclosure and US Patent 4,316,888 in the name of Nelson. The examiner finds obviousness based upon the acknowledgment in the specification that morphine is a known drug for treatment of pain and the teaching in Nelson that "contrary to the belief that dextromethorphan had no analgesic effect it has such an effect in the relief of gastrointestinal pain."

On April 30, 2003, the undersigned conducted a telephone interview with Examiner Criares. During the interview the aforementioned rejection was reviewed and the amendments set forth in this paper were discussed. The Examiner indicated that, subject to further review, the proposed amendment appeared to advance the prosecution of the application.

Applicants respectfully transverse the rejection of obviousness with respect to the previously pending claims 1-16 because Nelson does not suggest the specific combination of dextromethorphan with an addictive substance such as morphine or any benefit for the

combination However, Applicants submit this Amendment in an effort to further distinguish the claims and facilitate early reissuance.

In the Office Action, the Examiner suggested that the claims be amended to reflect that "applicants' NMDA receptor agents yield an enhanced effect to the composition " During the interview, the undersigned suggested a modification to the Examiner's proposed language. The terminology "enhanced effect" suggests that the effect of the nontoxic synthetic substance is to increase, make greater, heighten or intensify the effects of the addictive substance. This terminology is too limiting and does not embrace one of the benefits of the nontoxic synthetic substance as described in the specification, which is the reducing or inhibiting of a negative effect of an addictive substance such as morphine. For example, at Column 1, lines 28-35, addictive substances such as morphine are described as having negative side effects. The nontoxic synthetic substances are later described as improving the effect of the addictive substance by reducing the propensity of a mammal host from developing addictiveness or dependence to the addictive substance. The language proposed by applicants in the claims, that the nontoxic synthetic substance "provides an improved effect for the addictive substance if used alone," embraces the foregoing benefit of the nontoxic synthetic substance illustrated in the specification. See, e.g., Column 3, lines 40-47 and column 6 lines 55-57.

The present amendment adds this terminology in all of the independent claims previously presented, claims 1, 3, 4 and 5. As a result, the claims are limited to those compositions in which the nontoxic synthetic substance, e.g. dextromethorphan, provides an improvement in the effects provided by the addictive substance when used alone, i.e., without the nontoxic synthetic substance being present. There is no suggestion in the Nelson patent to combine dextromethorphan with an addictive substance and no suggestion that

dextromethorphan would provide any improved effects for an addictive substance when administered to mammals. For these reasons, the rejection of present claims 1 through 16 should be withdrawn and the claims found allowable.

Applicants also present three new claims, independent claims 16 and claims 17 and 18, which depend from claim 16. These claims exclude morphinans, e.g. dextromethorphan, from the composition. The patent specification provides basis for excluding the subclass of morphinans because it recognizes morphinans as a separate subclass of nontoxic synthetic blockers of the NMDA receptor. See, e.g., column 4, lines 51-56. These three claims are further distinguished from Nelson, because Nelson only discloses dextromethorphan. There is no reason to include in these claims the further element that the nontoxic synthetic substance provides improved effects to the addictive substance when used alone.

Applicants will submit a Supplemental Declaration by the named inventors with respect to the newly submitted and amended claims. Applicants respectfully request the Examiner to hold the requirement for a supplemental declaration in abeyance until the claims are found allowable.

In view of the amendment herein to the claims and the foregoing remarks it is believed all claims presented are patentable and allowance of this reissue application is respectfully solicited.

Applicants attach hereto as pages A1 to A4, a reproduction of all of the claims now presented in accordance with 37 C.F.R. § 1.173(c).

Applicants' attorney invites further communications with the Examiner, if it would expedite or facilitate the prosecution.

The Commissioner is hereby authorized to charge any additional fees which may be required for the timely consideration of this amendment under 37 C.F.R. §§ 1.16 and 1.17, or credit any overpayment to Deposit Account No. 13-4500, Order No. 3856-4006.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: May 2, 2003 By: _____
Arnold I. Rady
Registration No. 26,601

Correspondence Address:
MORGAN & FINNEGAN, L.L.P.
345 Park Avenue
New York, NY 10154-0053
Telephone 212-415-8552
Facsimile(212) 751-6849

Status Of The Claims Pursuant to 37 C.F.R. §1.173 (c)

1. (Twice Amended) A formulated pharmaceutical composition comprising an addictive substance and at least one nontoxic synthetic substance that blocks the N-methyl-D-aspartate receptor or a major intracellular consequence of N-methyl-D-aspartate receptor activation, that provides an improved effect to the composition and which excludes ketamine, AP-5 and 7-chlorokynurenate, the addictive substance being selected from the group consisting of alfentanyl, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, metazocine, methadone, metopon, morphine, opium extracts, opium fluid extracts, powdered opium, granulated opium, raw opium, tincture of opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan and pharmaceutically acceptable salts thereof.

2. (Original) The composition of claim 1 in sustained release dosage form.

3. (Currently Amended) A formulated pharmaceutical composition comprising an addictive substance and at least one nontoxic synthetic substance that provides an improved effect for the addictive substance if used alone and that blocks the N-methyl-D-aspartate receptor and consists essentially of a morphinan or blocks a major intracellular consequence of N-methyl-D-aspartate receptor activation, the addictive substance being selected from the group consisting of alfentanyl, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, metazocine, methadone, metopon, morphine, opium extracts, opium fluid extracts, powdered opium, granulated opium, raw opium, tincture of opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan and pharmaceutically

acceptable salts thereof.

4 (Currently Amended) A formulated pharmaceutical composition comprising an addictive substance and a non-toxic synthetic substance, the addictive substance being selected from the group consisting of alfentanyl, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, isomethadone, levorphanol, methadone, morphine, oxycodone, oxymorphone, pethidine, and pharmaceutically acceptable salts thereof, the non-toxic synthetic substance providing an improved effect for the addictive substance if used alone and being selected from the group consisting of dextromethorphan, dextrorphan, and pharmaceutically acceptable salts thereof.

5. (Currently Amended) A formulated pharmaceutical composition comprising an addictive substance and a non-toxic synthetic substance, the addictive substance being selected from the group consisting of alfentanyl, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, isomethadone, levorphanol, morphine, oxycodone, oxymorphone, pethidine, and pharmaceutically acceptable salts thereof, the non-toxic synthetic substance being a blocker of the N-methyl-D-aspartate receptor and consisting essentially of morphinans, and providing an improved effect for the addictive substance if used alone.

6. (Previously Added) A composition according to claims 1, 3, 4 or 5 wherein the addictive substance is selected from the group consisting of alfentanyl, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, isomethadone, methadone, morphine, oxycodone, oxymorphone, pethidine, and pharmaceutically acceptable salts thereof.

7. (Previously Added) A composition according to claims 1, 3, 4 or 5 wherein the addictive substance is selected from the group consisting of alfentanyl, codeine, dihydrocodeine, fentanyl, isomethadone, methadone, pethidine, and pharmaceutically acceptable salts thereof.

8. (Previously Added) A composition according to claims1, 3, 4 or 5 wherein the addictive substance is selected from the group consisting of codeine, methadone, and pharmaceutically acceptable salts thereof

9 (Previously Added) A composition according to claims 1, 3, 4 or 5 wherein the addictive substance includes morphine or a pharmaceutically acceptable salt thereof.

10. (Previously Added) A composition according to claims 1, 3, 4 or 5 wherein the addictive substance includes oxycodone or a pharmaceutically acceptable salt thereof.

11. (Previously Added) A composition according to claims 1, 3, 4 or 5 wherein the addictive substance includes hydrocodone or a pharmaceutically acceptable salt thereof.

12. (Previously Added) A composition according to claims 1, 3, 4 or 5 wherein the addictive substance includes oxymorphone or a pharmaceutically acceptable salt thereof.

13. (Previously Added) A composition according to claim 1, 3, 4 or 5 wherein the addictive substance includes hydromorphone or a pharmaceutically acceptable salt thereof.

14. (Previously Added) A composition according to claims 1, 3, 4 or 5, in oral dosage form.

15. (Previously Added) A composition according to claims 3, 4 or 5, in sustained release dosage form.

16. (Previously Added) A composition according to claims 1, 3, 4 or 5, in oral dosage and sustained release dosage form.

17. (New) A formulated pharmaceutical composition comprising an addictive substance and at least one nontoxic synthetic substance that blocks the N-methyl-D-aspartate receptor or a major intracellular consequence of N-methyl-D-aspartate receptor activation, and which excludes morphinans, ketamine, AP-5 and 7-chlorokynurenate, the addictive substance

being selected from the group consisting of alfentanyl, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, metazocine, methadone, metopon, morphine, opium extracts, opium fluid extracts, powdered opium, granulated opium, raw opium, tincture of opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan and pharmaceutically acceptable salts thereof.

18. (New) The composition according to claim17, wherein the nontoxic synthetic substance that blocks the N-methyl-D-Aspartate receptor is selected from pyrroloquinoline quinone and cis-4-(phosphonomethyl)-2-piperidinecarboxylic acid.

19. (New) The composition according to claim 17, wherein there is present a substance that blocks a major intracellular consequence of N-methyl-D-aspartate receptor activation.